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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/901,612	07/28/1997	BRUCE L. FRANK	HYZ-041FWC	9348

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EXAMINER

EPDS, JANET L

ART UNIT PAPER NUMBER

1635

DATE MAILED: 04/10/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/901,612

Applicant(s)

FRANK ET AL.

Examiner

Janet Epps

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,8-20,36,40-50 and 207-224 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1,8-20,36,40-50 and 207-224 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

2. Claims 1, 17, 19 and 40-44 remain rejected under 35 U.S.C. 102(b) as being anticipated by Wu et al. (both references cited in prior Office Action), for the reasons of record set forth in the Official Action mailed 6-01-2001, and those given below.

3. Claims 1, 13, 40-46, 48 and 50 remain rejected under 35 U.S.C. 102(e) as being anticipated by Carmichael, for the reasons of record set forth in the Official Action mailed 6-01-2001, and those given below.

Applicant's arguments filed 1-14-02 have been fully considered but they are not persuasive. Applicants traverse the above rejections over the Wu et al. references, and Carmichael reference on the grounds that neither reference anticipate independent claim 1 or any of the dependent claims since none of the references teach a oligonucleotide sequence selected from the group consisting of SEQ ID NOS 7-19 and 45. However, it is noted that the instant claims, as written, read on oligonucleotides that are complementary to a portion of the epsilon region of the HBV genome, wherein the region of the epsilon region consists of SEQ ID NO: 7-19 and 45. Applicants are invited to amend the claims with the appropriate punctuation to clarify that the sequences according to SEQ ID NO: 7-19 and 45 clearly read on the sequence of the claimed synthetic oligonucleotide, and does not refer to a portion of the epsilon region of the HBV genome. However, as written the instant claims recite wherein the sequences according to SEQ ID NO: 7-19 and 45 refer to a portion of the epsilon region of HBV, and not to the

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sequence of the claimed oligonucleotide. Moreover, it is noted that the claimed oligonucleotides need only be complementary to a "portion" of the epsilon region as defined by SEQ ID NO: 7-19 and 45. Therefore, the instant claims also encompass oligonucleotides complementary to only a portion of SEQ ID NO: 7-19 and 45 despite Applicant's amendment to the claims replacing the term "comprising" with the phrase "consisting of."

4. Claims 1, 8-14, 36, 40-46, 48-50 stand rejected under 35 USC 103(a) as being unpatentable over Korba et al. for the reasons of record set forth in the Official Action mailed 10/23/2000, and those arguments set forth below.

5. Claims 1, 8-20, 36, 40-46, 48-50, 207-213, 215-222 and 224 stand rejected under 35 USC 103(a) as being unpatentable over Korba et al. and further in view of Wu et al. (both references) for the reasons of record set forth in the official action mailed 10/23/2000, and those arguments set forth below.

6. Claims 1, 45 and 47 stand rejected under 35 USC 103(a) as being unpatentable over Korba et al. in view of Uhlmann et al. for the reasons of record set forth in the Official Action mailed 10/23/2000, and those arguments set forth below.

7. Claims 1, 17, 19, 212, 214, 220, 221, and 223 stand rejected under 35 USC 103(a) as being unpatentable over Korba and Wu et al. (either reference), as applied to claims 1, 17, 19, 212, 220, 221 above, and further in view of Uhlmann et al. for the reasons of record set forth in the Official Action mailed 10/23/2000, and those arguments set forth below.

8. Claims 1, 13, 40-46, 48, and 50 remain rejected under 35 USC 102(e) as being anticipated by Carmichael, for the reasons of record set forth in the Official Action mailed 10/23/2000, and those arguments set forth below.

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9. Claims 1, 8-20, 36, 40-50, 207-222 stand rejected under 35 USC 103(a) as being unpatentable over Carmichael in view of Uhlmann et al., or Carmichael taken together with Korba et al., Wu et al. (both references) and further in view of Uhlmann et al. for the reasons of record set forth in the Official Action mailed 10/23/2000, and those arguments set forth below.

Applicant's arguments filed 1-14-02 have been fully considered but they are not persuasive. Applicants traverse the instant rejections on the grounds that "none of the references either alone or in combination, teach or suggest the oligonucleotide of presently pending claim 1 wherein the oligonucleotide is selected from the group consisting of SEQ ID NOS 7-19 and 45." However, as stated above, the instant claims read on oligonucleotides that are complementary to a portion of the epsilon region of the HBV genome, wherein the region of the epsilon region consists of SEQ ID NO: 7-19 and 45, and do not read on wherein the oligonucleotides are selected from the group consisting of SEQ ID NOS: 7-19 and 45.

Additionally, Applicants argue that the cited art lacks suggestion or motivation to make the *particular* compounds now being claimed; general motivation is insufficient. However, contrary to Applicants assertions the cited references provide clear motivation to design oligonucleotides targeting the epsilon region of the HBV, for example Table 1 disclosed by Korba et al. shows that the oligonucleotides targeted to the epsilon portion of HBV were more active in inhibiting viral DNA levels than oligonucleotides targeted to other portions of the HBV sequence. Moreover, as stated in the prior Office Action, Carmichael provides general guidance and motivation to design oligonucleotides 20-25 nucleotides in length targeting nucleotides 1850 to 1910 of the HBV genome, the artisan would have at once envisaged oligonucleotides comprising the claimed sequences for testing. Furthermore, one would have been motivated to

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do so as a matter of routine experimentation to determine optimized antisense oligonucleotide sequences targeting the epsilon region as taught by Korba et al. and Carmichael. One would have had a reasonable expectation of success because Carmichael clearly shows that oligonucleotides targeted to different subsequences within the HBV epsilon target region have anti-HBV activity (Fig. 2).

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 8-20 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claims 8-20 and 36 recite wherein the claimed synthetic oligonucleotide is SEQ ID NO: 7-19 and 45. These claims are vague and indefinite since claim 1 recites wherein the sequence according to SEQ ID NO: 7-19 and 45 correspond to the epsilon region of the HBV genome. Applicants are invited to amend the language of claim to clearly recite wherein the sequences according to SEQ ID NO: 7-19 and 45 clearly read on the claimed synthetic oligonucleotides and not to the epsilon region of the HBV genome.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Epps, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Friday 8:30AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L Epps, Ph.D.
Examiner
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JLE
April 2, 2002


SEAN McGARRY
PRIMARY EXAMINER